

# Spectinomycin hydrochloride in the treatment of gonorrhoea: Its effect on associated *Chlamydia trachomatis* infections

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**SUMMARY** Sixty-three heterosexual men were successfully treated with a single injection of spectinomycin hydrochloride 2 g for urethral infections with *Neisseria gonorrhoeae*. *Chlamydia trachomatis* was recovered from the urethra of 11 of these men both before and after treatment. In six men, the organism was isolated after but not before treatment. No isolates were obtained from the remaining men either before or after treatment. All 17 of the men who yielded *C. trachomatis* developed post-gonococcal urethritis. Eight of 46 men from whom no isolate was obtained in their cultures developed post-gonococcal urethritis. Seventeen of 50 women successfully treated with spectinomycin for cervical infections with *N. gonorrhoeae* yielded isolates of *C. trachomatis* both before and after treatment. The organism was isolated from five women before but not after treatment, and from four women after but not before treatment. In 24 women culture for *C. trachomatis* was negative both before and after treatment. Spectinomycin hydrochloride in the dosage used rarely eliminated *C. trachomatis* from the genital tract of either men or women; in this respect it resembled two other drugs commonly used for the treatment of gonorrhoea—penicillin and ampicillin.

## Introduction

Patients with genital infections with *Neisseria gonorrhoeae* often have a concomitant infection with *Chlamydia trachomatis*. This organism, which is an important cause of non-gonococcal urethritis (Holmes, *et al.*, 1975; Oriel *et al.*, 1976a), has been isolated from 20 to 30% of men with gonococcal urethritis (Richmond *et al.*, 1972; Oriel *et al.*, 1976a) and from 30 to 60% of women with gonococcal cervicitis (Wentworth *et al.*, 1973; Hilton *et al.*, 1974; Oriel *et al.*, 1974). Several antibacterial agents in dosages that are curative for *N. gonorrhoeae* infections are ineffective against co-existing *C. trachomatis* infections. Thus gentamicin completely fails to eliminate *C. trachomatis* (Oriel

*et al.*, 1975), and both penicillin and ampicillin show only weak antichlamydial activity (Richmond *et al.*, 1972; Oriel *et al.*, 1976b). Most men with infection of the urethra by *C. trachomatis* which persists after treatment for gonorrhoea develop post-gonococcal urethritis (PGU) (Richmond *et al.*, 1972; Oriel *et al.*, 1975).

Spectinomycin, an aminocyclitol antibiotic, has given good results in the treatment of gonorrhoea (Cornelius and Domescik, 1970; Schroeter *et al.*, 1975), and has been recommended as the drug of choice for patients not cured by other antimicrobials (Venereal Disease Advisory Committee, 1974). Its clinical effect against *C. trachomatis* thus becomes important, although *in vitro* studies indicate only marginal activity (Ridgway *et al.*, 1976). We are reporting the effect of a single intramuscular injection of spectinomycin hydrochloride 2 g on *C. trachomatis* associated with *N. gonorrhoeae* in both men and women. Cell culture for *C. trachomatis* was performed before and after treatment in all

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Received for publication 20 May 1977

cases and the development of PGU in both *Chlamydia*-positive and *Chlamydia*-negative men was noted.

### Materials and methods

All patients were seen in the Department of Genito-Urinary Medicine, University College Hospital, London between August 1976 and February 1977, and informed consent was obtained before inclusion in the study. After local and general examination, specimens were collected as described below.

#### SPECIMEN COLLECTION FROM MEN

A specimen of urethral secretion was taken from each man with a disposable plastic loop and spread on a slide for Gram staining and microscopical examination. A second specimen was inoculated on to a selective culture medium for *N. gonorrhoeae*. A cotton-wool tipped wire endourethral swab was then inserted 4-5 cm into the urethra. On withdrawal, the swab was transferred to 2 ml of transport medium for *C. trachomatis*. A two-glass urine test was carried out at each visit, and serological tests for syphilis were also performed.

#### SPECIMEN COLLECTION FROM WOMEN

Women were examined in the lithotomy position. The cervix was exposed with a Cusco speculum. Urethral and cervical specimens for microscopical examination and culture for *N. gonorrhoeae* were taken using plastic disposable loops. A specimen from the posterior vaginal pool was also taken for microscopy and culture for *Trichomonas vaginalis*. The cervix was then cleaned with cotton-wool, and a cotton-wool tipped swab rotated in the cervical canal. On removal, the swab was transferred to 2 ml of transport medium for culture for *C. trachomatis*. Rectal specimens for culture for *N. gonorrhoeae* were taken from some patients, but cultures for *Chlamydia* were not performed on rectal specimens. Serological tests for syphilis were included for all patients.

In cases in which gonorrhoea was diagnosed, the patient (male or female) was given 2 g spectinomycin hydrochloride by intramuscular injection. Each patient was asked to return for re-examination after 3 days, 7 days, and 14 days. There was some individual variation in follow-up attendance, but in many cases it was possible to follow-up patients for longer periods. At each attendance the diagnostic tests described above were repeated. Patients were requested to refrain from sexual intercourse during the follow-up period.

#### ASSESSMENT OF PGU

PGU was defined as the presence of  $\geq 20$  polymorphonuclear leucocytes in at least three fields of a Gram-stained urethral smear examined at a magnification of  $\times 900$  (Oriel *et al.*, 1975).

#### LABORATORY METHODS

*N. gonorrhoeae* was cultured on a selective medium (Phillips *et al.*, 1972). Cell culture for *C. trachomatis* was by the method of Reeve *et al.* (1975), using McCoy cells pre-treated with idoxuridine.

### Results

#### MEN

A group of 114 heterosexual men with gonococcal urethritis was treated. Of these men, 51 were excluded for the following reasons: default (38), initial contaminated *Chlamydia* culture (8), treatment failure at first follow-up examination (1), reinfection with *N. gonorrhoeae* during follow-up (4). Thus, full results were available for 63 men. Cultures for *C. trachomatis* were positive at the initial visit in 11 (17.5%) of these men. A further six men yielded isolates during follow-up, for an overall isolation rate of 27.0% (Table 1).

Table 1 *Effect of a single dose of spectinomycin (2 g intramuscularly) on the frequency of isolations of Chlamydia trachomatis and on the development of post-gonococcal urethritis (PGU) in 63 heterosexual men with gonococcal urethritis*

Isolate of <i>C. trachomatis</i> cultured		No. of patients developing PGU/ no. with isolation pattern
Before treatment	After treatment	
Yes	Yes	11/11
Yes	No	0/0
No	Yes	6/6
No	No	8/46

Cultures for *C. trachomatis* were positive both before and after treatment in 11 patients. The intervals between isolations were one week or less for six men, two weeks for four men, and three weeks for one man. No patient who initially yielded *C. trachomatis* became isolation-negative after treatment. Six patients who were initially isolation-negative became isolation-positive after treatment, the intervals being one week for one man, two weeks for one man, and three weeks for four men. In 46 patients, isolates of *C. trachomatis* were not obtained before or after treatment; 13 of this group were followed-up for two weeks, 16 for three weeks, and 17 for four weeks.

After treatment with spectinomycin, 25 of the 63 patients with gonococcal urethritis (39.7%) developed PGU. All 17 men with positive cultures for *C. trachomatis* after treatment and eight of 46 men with negative cultures (17.4%) developed PGU.

#### WOMEN

A series of 55 women with confirmed gonococcal cervicitis was treated, but five were excluded (default (3), reinfection with *N. gonorrhoeae* during follow-up (1), initial contamination (1)). There were no treatment failures. Thus, results were available for 50 women (Table 2). Of these, 22 (44%) yielded *C. trachomatis* from the cervix on first examination and a further four during follow-up for an overall isolation rate of 52%. *C. trachomatis* was isolated from 17 women both before and after treatment. The intervals between examinations were one week or less for three women, two weeks for six women, three weeks for three women, and four weeks or more for five women. *C. trachomatis* was isolated from five patients before treatment but not subsequently, the intervals being two weeks (1 woman), three weeks (1 woman), and four weeks (3 women). *C. trachomatis* was not isolated from four patients before treatment but was isolated subsequently, the intervals being one week (1 woman), three weeks (2 women), and over four weeks (1 woman). Finally, *C. trachomatis* was not isolated from 24 women either before or after treatment, with intervals between examinations of two weeks (7 women), three weeks (3 women), and over four weeks (14 women).

Table 2 *Effect of a single dose of spectinomycin (2 g intramuscularly) on the frequency of isolation of Chlamydia trachomatis from the cervix of 50 women with gonococcal cervicitis*

Isolate of <i>C. trachomatis</i> obtained		
Before treatment	After treatment	No. of patients
Yes	Yes	17
Yes	No	5
No	Yes	4
No	No	24

#### Discussion

Spectinomycin in the dosage used was an effective treatment for gonorrhoea in our patients and had a low failure rate. However, this antimicrobial had little effect on associated *C. trachomatis* infection in either men or women; in this respect it resembled

penicillin and ampicillin.

The failure of the three agents which are the most widely used for the treatment of gonorrhoea to have a significant effect on associated *C. trachomatis* infection indicates an unsatisfactory situation. *C. trachomatis* is an important genital pathogen. It undoubtedly causes many infections of non-gonococcal urethritis, cervicitis, and neonatal eye disease (Dunlop *et al.*, 1966; Rees *et al.*, 1977); it may be implicated in the pathogenesis of salpingitis (Mardh *et al.*, 1977), epididymitis (Harnisch *et al.*, 1977), and neonatal respiratory disease (Beem and Saxon, 1977). Its treatment appears to be desirable. Between 20 and 60% of patients with gonorrhoea are infected by *C. trachomatis*, but at present only a proportion of the men (those diagnosed as having PGU) and none of the women are likely to receive effective treatment.

Because of the appearance of  $\beta$ -lactamase producing strains of *N. gonorrhoeae*, the treatment of gonorrhoea is at present being reappraised. Whether one drug will be found which gives good results in the treatment of both *N. gonorrhoeae* and *C. trachomatis* infections remains to be seen, but the time is ripe for further trials of antimicrobials, single, combined, or perhaps sequential, in the treatment of these serious infections.

We are grateful to Dr E. Joan Stokes for kindly providing laboratory facilities and to Ms Lam Po Tang for technical assistance. This work was supported by the Medical Research Council and by Upjohn Ltd.

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